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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,651	01/27/2004	Ronald A. Beyerinck	PC23195B	4574
28523 7590 04/23/2007 PFIZER INC. PATENT DEPARTMENT, MS8260-1611 EASTERN POINT ROAD GROTON, CT 06340			EXAMINER SASAN, ARADHANA	
			ART UNIT	PAPER NUMBER
			1609	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		04/23/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

Application No.

10/766,651

Applicant(s)

BEYERINCK ET AL.

Examiner

Aradhana Sasan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 1-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 03/29/2004.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Status of Application***

1. Claims 1-21 were "withdrawn" (Amendment of the claims 01/27/2004). However, if applicant's intention was to cancel the claims, applicant should correct this term to be "cancelled" since these were claims from the parent application (10/353,746).
2. Claims 22-43 are being presented for examination.

### ***Information Disclosure Statement***

3. The information disclosure statement (IDS) submitted on 03/29/2004 was filed. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement. See attached copy of PTO-1449.

### ***Double Patenting***

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 22-43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 21 in view of claims 1, 7-16, 17-20 of U.S. Patent No. 6,763,607 ('607 hereafter). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claim 21 of '607 is the product of any of the process claims 1-20. Therefore, a composition comprising an amorphous dispersion of a drug and a polymer of instant claims 22-43 would not be patentable over claim 21 in view of claims 1, 7-16, 17-20 of '607.

Instant claim 22 would have been obvious to a person having ordinary skill in the art over claim 21, in view of claims 1, 11 and 13 of '607. The claim limitations of amorphous dispersion comprising a drug and a polymer, and at least 80% of the particles having a diameter greater than 10 $\mu$ m are recited in the reference claims. Although the claim limitations of average particle diameter of 40 $\mu$ m and bulk specific volume of less than 5ml/g are not specifically taught in the reference claims, a person having ordinary skill in the art would have arrived at particle diameter and bulk specific volume values during the process of routine experimentation and optimization.

The claim limitation of particle diameter of instant claim 23 would have been obvious to a person having ordinary skill in the art over claim 21, in view of claim 12 of '607. Claim 12 of '607 recites the particle diameter of greater than 10 $\mu$ m.

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As mentioned above, the claim limitations of average particle diameter of 40 $\mu$ m and bulk specific volume of less than 5ml/g of instant claims 24 and 25 are not specifically recited in the claims of '607, but a person having ordinary skill in the art would have arrived at particle diameter and bulk specific volume values during the process of routine experimentation and optimization.

The drug selection limitation of instant claims 26-27 would have been obvious over claim 21 in view of claims 17 and 18 of '607.

The polymer selection limitation of instant claims 28-30 would have been obvious over claim 21 in view of claims 19-20 of '607.

The drug and polymer selection limitations of instant claim 31 would have been obvious over claim 21 in view of claims 18-20 of '607.

The amorphous dispersion and homogenous dispersion limitations of instant claim 32 would have been obvious over claim 21 in view of claim 13 of '607.

The concentration enhancing polymer limitation of instant claim 33 would have been obvious over claim 21 in view of claim 1 of '607.

The drug concentration enhancement limitation of instant claims 34-35 would have been obvious over claim 21 in view of claim 14 of '607.

The area under the curve increase (1.25 fold) limitation of instant claim 36 would have been obvious over claim 21 in view of claim 15 of '607.

The bioavailability increase (1.25 fold) limitation of instant claim 37 would have been obvious over claim 21 in view of claim 16 of '607.

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The dispersion formed by spray drying process limitation of instant claim 38 would have been obvious over claim 21 in view of claim 1 of '607.

The particle diameter and  $D_{10}$  limitation of instant claim 39 would have been obvious over claim 21 in view of claims 7 and 8 of '607. Although the claims of '607 do not specifically recite the average particle diameter of at least  $50\mu\text{m}$ , a person having ordinary skill in the art would have arrived at that particle diameter by using the spray drying process and components taught by '607 during the process of routine experimentation and optimization.

The  $D_{90}$  limitation of instant claims 40 and 41 would have been obvious over claim 21 in view of claims 7 and 8 of '607. Although the claims of '607 do not specifically recite the  $D_{90}$  values, a person having ordinary skill in the art would have arrived at these values of diameter of particles that make up 90% of the volume during the process of routine experimentation and optimization.

The span limitations of instant claims 42-43 would have been obvious over claim 21 in view of claims 9 and 10 of '607.

Since the instant application claims a composition comprising a drug and a polymer made by a process of spray drying, it is obvious over the claims of '607 and thus they are not patentably distinct over each other.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 22-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curatolo et al. (US 2002/0103225, '225 hereafter).

The claimed invention is a composition comprising an amorphous dispersion of a drug and a polymer made by spray drying. The particles of the dispersion have an average diameter of at least 40 $\mu$ m, a bulk specific volume of less than 5ml/g, and at least 80 vol% of the particles having a diameter greater than 10 $\mu$ m.

'225 teaches a pharmaceutical composition comprising a solid amorphous dispersion of a drug (a cholesteryl ester transfer protein inhibitor) and a polymer (a concentration enhancing polymer).

'225 does not expressly teach that the particles have an average diameter of at least 40 $\mu$ m, a bulk specific volume of less than 5ml/g, and that at least 80 vol% of the particles have diameters of greater than 10 $\mu$ m.

A person having ordinary skill in the art at the time the invention was made would have found instant claim 22 obvious over '225. '225 teaches a solid amorphous dispersion of a drug and a polymer (Abstract). The dispersion is formed by "solvent processing" and an exemplary process is spray drying (Page 34, [0560]). "Droplet sizes range from 1 $\mu$ m to 500 $\mu$ m in diameter, with 5 to 100 $\mu$ m being more typical" (Page 34,

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[0563]). '225 further teaches that the preferred "size of droplets formed during the spray-drying process are less than about 100 $\mu$ m in diameter" (Page 34, [0563]). Therefore, the limitations of average diameter of at least 40 $\mu$ m and at least 80 vol% of particles having diameters greater than 10 $\mu$ m of instant claim 22 would have been obvious to one skilled in the art given the particle sizes taught by '225. The bulk specific volume limitation of instant claim 22 would have been obvious to one skilled in the art as a further measurement (of the flow characteristics) of the spray dried particles and the value of less than 5ml/g would be a result of the measurement.

Similarly, the particle diameter limitation of instant claims 23-24 and the bulk specific volume limitation of instant claim 25 would have been obvious to one skilled in the art given the particle size teaching of '225.

The drug selection limitation of instant claims 26-27 would have been obvious to one skilled in the art over '225. '225 teaches a CETP inhibitor (cholesteryl ester transfer protein inhibitor) as the drug in the composition (Abstract). '225 teaches [2R,4S] 4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester (Page 14, [0182] and Page 53, claim 18).

The polymer selection limitation of instant claims 28, 29, and 30 would have been obvious to one skilled in the art over '225. Regarding instant claim 28, '225 teaches ionizable non-cellulosic polymers (Page 31, [0540]), ionizable cellulosic polymers (Page 31, [0542] and Page 68, claim 49). Regarding instant claim 29, '225 teaches hydroxypropyl methyl cellulose as a polymer (Page 32, [0546] and Page 68, claim 51).

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Regarding instant claim 30, '225 teaches hydroxypropyl methyl cellulose acetate succinate (Page 32, [0549] and Page 68, claim 52).

The drug and polymer of instant claim 31 would have been obvious to one skilled in the art over '225 which teaches [2R,4S] 4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester (Page 14, [0182] and Page 53, claim 18) and hydroxypropyl methyl cellulose acetate succinate (Page 32, [0549] and Page 68, claim 52).

The "substantially amorphous" drug and "substantially homogenous" dispersion limitations in instant claim 32 would have been obvious to one skilled in the art over '225 which teaches that the drug (the CETP inhibitor) in the dispersion is "substantially amorphous" (Page 3, [0026] and Page 45, claim 6) and "the dispersion is preferably substantially homogenous so that the amorphous CETP inhibitor is dispersed as homogeneously as possible throughout the polymer" (Page 3, [0028] and Page 46, claim 8).

The concentration enhancing polymer of instant claim 33 would have been obvious to one skilled in the art over '225 which teaches a concentration enhancing polymer in the dispersion (Abstract).

The concentration enhancement of the drug by the concentration enhancing polymer of instant claim 34 would have been obvious to one skilled in the art over '225 which teaches concentration enhancement of the drug (the CETP inhibitor) in *in vitro* tests (Page 3, [0030]) and in *in vivo* tests ("when dosed orally to a human or other animal") (Page 4, [0036]). It is also taught that the concentration enhancing polymer is

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present in an amount sufficient to enhance the concentration of the drug in a use environment (Page 68, claim 56).

The maximum drug concentration enhancement of at least 1.25 fold of instant claim 35 would have been obvious to one skilled in the art over '225 which teaches compositions that "provide a Maximum Drug Concentration (MDC) that is at least 10-fold the equilibrium concentration of a control composition" (Page 4, [0031]).

Regarding instant claim 36, the composition providing an area under the drug concentration versus time curve that is at least 1.25 fold that of a control composition would have been obvious to one skilled in the art over '225. '225 teaches a composition which provides a concentration versus time area under the curve at least 5-fold that of a control composition (Page 4, [0032]).

Regarding instant claim 37, the composition providing a relative bioavailability of the drug that is at least 1.25 fold that of control composition would have been obvious to one skilled in the art over '225 which teaches that the "relative bioavailability of the test composition is at least about 4 relative to a control composition" (Page 5, [0038]).

Regarding instant claim 38, the composition made by the process of spray drying would have been obvious to one skilled in the art over '225 which teaches that the dispersion is formed by "solvent processing" and an exemplary process is spray drying (Page 34, [0560] and Page 69, claims 86 and 87). '225 teaches "dissolution of the CETP inhibitor and one or more polymers in a common solvent" (Page 34, [0560]), removal of solvent through the process of spray drying, atomization, and mixing the liquid droplets with a warm drying gas (Page 34, [0561]).

Regarding instant claims 39, 40, and 41, the average diameter,  $D_{10}$  and  $D_{90}$  limitations would have been obvious to one skilled in the art over '225 which teaches that "droplet sizes range from  $1\mu\text{m}$  to  $500\mu\text{m}$  in diameter, with 5 to  $100\mu\text{m}$  being more typical" (Page 34, [0563]). '225 further teaches that the preferred "size of droplets formed during the spray-drying process are less than about  $100\mu\text{m}$  in diameter" (Page 34, [0563]). A person with ordinary skill in the art at the time the invention was made would modify the process parameters during the process of routine experimentation and optimization to arrive at the average droplet diameter of at least  $50\mu\text{m}$ , a  $D_{10}$  of at least  $10\mu\text{m}$ , a  $D_{90}$  of less than about  $300\mu\text{m}$ , and a  $D_{90}$  of less than about  $250\mu\text{m}$  since '225 teaches a droplet size range from  $1\mu\text{m}$  to  $500\mu\text{m}$ . See MPEP 2144.05.

The span limitation of instant claims 42 and 43 would have been obvious to one skilled in the art over '225 which teaches the particle diameter ranges (as stated above). One skilled in the art could calculate the span given the  $D_{10}$ ,  $D_{50}$  and  $D_{90}$  figures.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising an amorphous dispersion of a drug and a polymer by spray drying, as suggested by '225, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because this composition allows enhancement of the drug concentration, and consequently enhancement of drug bioavailability.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re*

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*Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Conclusion***

1. No claims are allowed.
2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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Business Center (EBC) at 866-217-9197 (toll-free).



**VICKIE KIM**  
**PRIMARY EXAMINER**